

FOR THE MEDICAL PROFESSION ONLY.

Seventh Bulletin, Sept., 1925.

DETOXICATED VACCINES

*New Detoxicated Vaccines against Influenza
and Coryza.*

(B. Pneumosintes and other organisms.)

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P.O. Box No. 652.

143-5, Great Portland Street,
London, W.1.

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Important Discoveries Regarding Influenza & Coryza.

IN 1920 there was reported from the Rockefeller Institute, New York, the discovery of a new filter passing germ which was believed to be the true cause of epidemic influenza. This new organism was called by Olitsky and Gates, the discoverers, **Bacterium pneumosintes**. Although it has not yet been entirely accepted by bacteriologists that this germ is the true cause of influenza, nevertheless, the accumulated evidence points very strongly to the incrimination of this minute organism. Further important evidence has recently been published in the Annals of the Pickett-Thomson Research Laboratory, Vol. I., No. 2, June, 1925, and in the Proceedings of the Royal Society of Medicine, Vol. 18, No. 7, May, 1925. Thus the germ was found in several cases of influenza occurring in England, and was also isolated from a case of Engadine Fever occurring in Switzerland. Engadine fever is regarded by the doctors in the Engadine as a variety of influenza.

Up to this time the organism had only been cultivated with very great difficulty, and the amount of germ emulsion obtainable was so small that no vaccines of this bacterium were available. Towards the end of 1924 a very satisfactory culture medium for growing the germ easily was discovered in the Pickett-Thomson Research Laboratory. At this time, however, the quantity of germs available was too small for the purpose of producing sufficient detoxicated vaccine, so the ordinary toxic variety of vaccine was first prepared.

It was found that this ordinary **B. pneumosintes** vaccine was extremely toxic, producing symptoms like influenza when the dose injected was 50 millions or greater. A considerable amount of this toxic vaccine was sent out to the medical profession for trial, and good reports as to its value were obtained. Since that time a large quantity of the germ has been cultivated and a considerable quantity of detoxicated **B. pneumosintes** vaccine has now been prepared.

Experiments carried out in the laboratory have shown that doses of 5,000 millions of the detoxicated vaccine can be given without harmful symptoms. This dosage is two hundred times greater than the dosage recommended in the case of the toxic vaccine. The chemicals used in the detoxication of this organism are so weak, namely, N/200 to N/1000 NaOH and N/1000 HCl that no possible damage can be done to the antigenic properties of the vaccine. There is every reason to believe therefore, that this vaccine will be at least 100 times more efficient as an immunising agent than the ordinary toxic vaccine.

We cannot do better than quote the following abstract from the Annals of the Pickett-Thomson Research Laboratory, Vol. 2, No. 1, Aug., 1925:—

“In the Annals of the Pickett-Thomson Research Laboratory, Vol. 1, No. 2, p. 248, the writers have already given their experiences with the ordinary toxic vaccines prepared from **B. pneumosintes** (Olitsky and Gates strains). This vaccine was found to be extremely toxic, doses of 50

millions producing malaise, depression, and muscular weakness. After a total dosage of 80 millions no detectable agglutinins or complement fixing substances could be found in the blood.

Considerable quantities of this toxic vaccine were sent to various doctors for trial in their practice, and several reports have been received from them giving their experiences with it. One medical man who was a martyr to recurrent influenzal attacks, derived great benefit from a course of nine injections varying in dosage from 5 millions to 20 millions.

The following is an extract from his letter:—

‘You may be interested to know how I personally have got on with the **B. pneumosintes** vaccine. I have had nine injections as follows:—

			<i>Reaction.</i>
Feb. 18	5	mill. B. Pueumosintes.	Felt chilly two days.
„ 21	7½	„ „	No „ „ „ „
„ 28	10	„ „	No reaction.
Mar. 8	20	„ „	„ „
„ 15	20	„ „	„ „
„ 22	20	„ „	„ „
„ 29	20	„ „	„ „
Apr. 4	20	„ „	„ „
May 3	20	„ „	„ „

I can only believe it is my germ, as I have not felt better for years, in fact, since before I was mustard gassed on September 3rd, 1917. I have lost all my peculiar feelings of being on the verge of a temperature, pains in the calves and shoulders and general malaise—in short, a kind of “chronic influenza.” I hope I am correct in my surmise

and shall continue the injections at two or three weekly intervals. Next winter will be the test, and I shall be only too pleased to let you know how I go on. I may say, which is interesting, that I have had a cold in the head for a short period during this long course of injections, the symptoms were purely local and I felt quite fit during this coryza, and it went away after a few days.'

Another physician reports that he has used the toxic **B. pneumosintes** vaccine in the treatment of over fifty cases of influenza, with exceptionally good results. He considered that doses of four to five millions injected subcutaneously were the best, and often had a marked effect in alleviating the troublesome cough.

Reports on the value, if any, of small doses of the toxic vaccine as a preventative inoculation against influenza have not yet been received.

The results obtained by Olitsky and Gates in this direction do not appear so far to have been very satisfactory. One of us in spite of three injections amounting to a total of 80 millions, contracted a very mild attack of influenza in Switzerland about one month later. The temperature on this occasion did not rise higher than 99.5° F., and only lasted one day. It is possible, therefore, that the mildness of the attack was due to some resistance acquired as a result of the previous vaccine inoculation. At any rate it is hardly likely that successful

prophylaxis can be obtained with such small doses, and unfortunately only small doses can be given on account of the great toxicity of the vaccine.

Detoxicated Vaccines Prepared from *B. Pneumosintes*.

RECENTLY the authors have cultivated a sufficient amount of the germ to enable them to prepare considerable quantities of detoxicated *B. pneumosintes* vaccine. This organism dissolves very much more easily in alkali than any other germ so far known. We have found that it will dissolve very rapidly at blood heat in two-hundredth normal NaOH, and with the aid of the vaccine churns described in Vol. 1 of this Journal it can be dissolved even in one-thousandth normal NaOH.

In a previous paper published in this Journal, Vol. 1, p. 187, we pointed out that the antigenic properties of sheep red corpuscles were not injured by treatment with N/50 to N/100 NaOH. It is extremely unlikely, therefore, that still weaker alkali, *viz.*, N/200 NaOH, should have the slightest deleterious action on the antigenic properties of *B. pneumosintes*.

Our process of detoxicating this organism is as follows:—

(1) Dissolve the germ in N/200 to N/1000 NaOH at 37.5° C. The solution is complete in half an hour.

(2) Filter the solution through a Berkefeld filter.

(3) Add a few drops of very dilute HCl to bring the solution to pH=5 (this is less than 1000th normal acidity, which is even incapable of injuring the complement of blood serum). At this reaction the pneumosintes protein is precipitated, and the precipitate is removed by centrifuging.

(4) The pneumosintes precipitate is washed in normal saline and standardised to a strength of 10,000 to 50,000 millions per c.c.

It will be noted that the strongest chemical used in this gentle detoxication process is N/200 NaOH. No other chemical is used except HCl at a strength of less one-thousandth normal. Even the most fastidious must admit that this process cannot possibly damage the antigenic properties of the vaccine.

As we had never before used such weak alkali in the detoxication of vaccines, it remained to be ascertained if the detoxication was successful. By inoculation experiments it was found that this vaccine was quite as non-toxic as those others wherein much stronger alkali is used in the process.

We have ascertained, therefore, that by the use of no stronger chemical than N/200 NaOH, the extremely toxic properties of **B. pneumosintes** can be removed to such an extent that doses several hundred times as great as the toxic vaccine can be given without harmful reactions.

It has recently been proved that diphtheria toxin can be rendered non-toxic without destroying its properties as an antigen in the production of diphtheria anti-toxin. Bacteriologists are, therefore, coming round to the view which has long since been held by one of us that the actual toxin of bacteria is not of any material importance in the production of immunity. If this is true then the principle of detoxication is correct, since a greater immunity will be obtained by the greatly increased dosage, and as no harmful toxic reactions occur, these larger doses can be administered to patients even in the acute stages of the disease. It would appear, therefore, that there is very good reason to hope that if **B. pneumosintes** should prove definitely to be the cause of influenza, then we will have in the detoxicated vaccine a very successful remedy for the prevention and treatment of this extremely harmful disease.

The following blood tests which we have carried out upon ourselves during a course of inoculations with detoxicated **pneumosintes** vaccine show very clearly that the resulting anti-substance produced is much greater than that obtained after the extremely small doses of the toxic vaccine.

We have already mentioned that no detectable anti-substances could be found in our blood serum as ascertained by the complement fixation and agglutination tests after three doses of the toxic **B. pneumosintes** vaccine amounting to a total of 80 million germs.

After this we inoculated ourselves with successively increasing doses of a detoxicated

B. pneumosintes vaccine, prepared as described above. The doses which we injected into each other were 100 mils., 250 mils., 500 mils, 1,000 mils., 2,000 mils., and 4,000 mils. respectively, amounting in all to a total of 8,000 millions. As a result of these inoculations our blood serum which previously had given negative results to the complement fixation test, now gave a double positive result with a **B. pneumosintes** antigen. The test was repeated three times with the same results, control sera being always negative.

These preliminary experiments would appear to show that the large doses of the detoxicated vaccine are superior as an immunising agent to the much smaller doses of the toxic vaccine."

In view of the above researches we have prepared a new **detoxicated Anti-Influenza** vaccine of the following composition:—

<i>B. pneumosintes</i>	..	..	..	10,000	mils.	per	c.c.
<i>B. influenza</i> (Pfeiffer)	..	..	..	10,000	"	"	"
<i>Pneumococcus</i> (types I., II., III. & IV.)	10,000	"	"	"	"	"	"
<i>Hæmolytic streptococcus</i>	..	..	..	10,000	"	"	"
TOTAL				40,000	mils.	per	c.c.

Particulars of dosage for treatment and prophylaxis will be found on page 21 of this *Bulletin*.

New Detoxicated Anti-Coryza Vaccine.

As a result of extensive researches on the bacteriology of the respiratory tract, some ten new species of bacteria have been discovered in cases of bronchial and nasal catarrh. We have therefore added a certain number

of these new organisms to our new Coryza vaccine, which now has the following composition:—

<i>New Organisms</i>	10,000	million	per c.c.
<i>B. pneumosintes</i>	5,000	„	„
<i>Pneumococci</i> (four types)	5,000	„	„
<i>M. catarrhalis</i>	5,000	„	„
<i>B. Friedlander</i>	5,000	„	„
<i>B. septus Hofmann</i>	5,000	„	„
<i>Staphylococci</i>	5,000	„	„
<i>Hæmolytic streptococci</i>	5,000	„	„
<i>B. influenzae</i> (Pfeiffer)	5,000	„	„
TOTAL	50,000	million	per c.c.

Particulars of dosage for treatment and prophylaxis will be found on page 20 of this *Bulletin*.

New Suggestions for the Treatment of Whooping Cough.

We have permission to give the following details for the treatment of Whooping Cough in children, by a physician who has used our detoxicated Whooping Cough vaccine with striking success:—

“CHILD AGED 5 YEARS.

Open air treatment and rest as far as conveniently possible.

Give subcutaneous injections of the detoxicated vaccine in upper part of buttock with child lying face downwards across parent's lap and playing with new toy.

Give 2/10, 3/10, 4/10, 5/10 c.c. at intervals of four, five and six days respectively, *e.g.*, on 1st, 5th, 10th and 16th of month.

Don't give any other drugs or liniments, except for two days after first injection give a little bromide. One thus visits four times only and finishes attendance in 16 days.”

The Advantages of Detoxicated Vaccines

- (1) They are highly antigenic (immunising) and non-toxic.
- (2) Large doses can be given without severe or poisonous reactions, and a very high state of immunity is thereby produced without inconvenience; thus, in the case of anti-typhoid or anti-influenza inoculation, the symptoms produced are so mild that the inoculated person is not incapacitated in the least for even one day.
- (3) Inoculations with detoxicated vaccines are practically never followed by general toxic symptoms. Any reaction produced is usually only local.
- (4) They are specially suitable for administration in acute febrile infections, since the inoculations increase the immunity without aggravating the toxic symptoms of the disease. Thus large doses of detoxicated gonococcal vaccine can be given with great advantage in the earliest acute stages of gonorrhœa. Equally satisfactory results are obtained with moderate doses in other acute diseases, such as typhoid fever, puerperal fever, influenza, and acute infective catarrhs, etc.
- (5) Such infections are not aggravated by the appropriate doses, and the duration of the disease is considerably shortened.

Instructions regarding Dosage of Detoxicated Vaccines

THE susceptibility of different individuals towards vaccines, varies in a very remarkable manner; in consequence, it is impossible to lay down a hard and fast rule as to dosage. On this account it is good practice to begin in all cases with a small dose in order to ascertain if there is any particular idiosyncrasy or susceptibility. This care is more especially advisable in weak subjects suffering from an acute febrile condition. If, after two days, it is found that the small test dose has had no effect whatsoever, as is usually the case, give double the original dose at the end of the second day.

In acute cases with fever where there is considerable urgency, the interval between non-reactive doses should be about three days, and so long as no fever reaction (indicated by a rise in temperature) is produced by any injection, the subsequent injection may be increased considerably even to double the preceding dose. If, on the other hand, a reaction is produced which is considered to be too severe, then it is advisable to give the patient a rest of five days, and the next dose should rather be reduced than increased.

In the vast majority of cases it will be found that the initial doses of detoxicated vaccine recommended by us, may be given without fear even to the most susceptible patients. Nevertheless, in all instances the

physician must use his own experience and judgment. In our table of dosage quoted elsewhere in this booklet, we give two separate series of inoculations for most of the varieties of vaccines. One series gives the dosage recommended for acute cases with fever, and the other series of larger doses is that recommended for chronic cases without fever. As a general rule it may be stated that patients with fever should receive one-half the dosage that is given to non-febrile cases. Different kinds of germs are not equally detoxicated by the process, so there is no uniform dosage for all detoxicated vaccines. Moreover, when a patient is susceptible to one variety of vaccine, he is not necessarily susceptible to another variety.

In many instances much larger doses of detoxicated vaccine can be given than the maximum doses which we give elsewhere in the list. We have records of cases wherein the dosage of detoxicated gonococcal vaccine has been increased rapidly up to 50,000 millions. In certain patients with chronic bronchial and nasal catarrh, the dose of our coryza vaccine may be increased to a similar degree with advantage to the patient.

The dosage of detoxicated vaccine, which we recommend in the list is based on wide clinical experience in many and varied types of cases, covering the bacterial infections amenable to vaccine treatment. Nevertheless, the doses which we recommend serve only as a guide, and it is left to the discretion of the physician as to whether larger or smaller doses should be given in any individual case.

The Intervals between Doses of Vaccine

WHEN a vaccine of a given germ is injected under the skin, say of the upper arm, a temporary inflammation is produced at the site of injection. This inflammation of the local tissues commences to appear some four or five hours after the inoculation, and continues for about twenty-four hours. This local reaction, as it is called, may be very slight and scarcely noticeable. With detoxicated vaccines, a general toxic reaction with rise of temperature seldom occurs. Nevertheless, even with this vaccine there is a slight negative phase for the first twenty-four hours, as can be estimated by the blood tests. A further injection of vaccine should never be administered until the negative phase is past, and good results could hardly be expected from injections administered every day or even every two days.

If there is a very slight reaction, it may be taken that the negative phase will pass quickly (in twenty-four hours), and after allowing two more days to elapse, the next dose may be administered on the third day. Where an appreciable reaction occurs, it is advisable not to give the next dose until the fifth day, and where the reaction is very severe, a considerable rest should be given amounting to seven or even ten days. In other words, when small doses are given with no reaction, the intervals can be cut down to three days; when large doses are given and where there is considerable reaction, the intervals should be increased to five, seven or even ten days in order to reap the benefit of the positive phase.

The Increase of the Dosage

IN chronic cases without fever, the dosage may be increased rapidly by doubling the amount of each successive injection. In acute febrile diseases, the increase should be more cautious.

The Dosage for Infants and Children

THE doses which we have tabulated elsewhere have been compiled for the average adult weighing 140 lbs. (10 stone). In the case of children, the doses should be reduced in proportion to their body weight. For example, a child weighing 28 lbs. would require one-fifth of the dose recommended for the adult, while a child of 14 lbs. would require one-tenth of the adult dose.

Site of Injection

WE usually recommend subcutaneous injections, but some doctors prefer to give the vaccine intramuscularly. When given by the latter method, the resulting local tenderness and redness is not so visible. On the other hand, the advantage of the subcutaneous method is that one can judge the amount of local reaction more easily. Any site may be chosen where the skin is loose, and the subcutaneous tissue is abundant. A very convenient situation is the loose tissue around the upper arm.

For intramuscular injection the buttock, the thigh, or the deltoid may be chosen. It is good practice to vary the site of the injections. It is better to do so than to inject always into the same spot.

Varieties of Detoxicated Vaccine

Detoxicated Gonococcal Vaccine (A).

(Telegraphic code: "Puregon.")

THIS is a pure gonococcal vaccine prepared from many strains (polyvalent). It is indicated in all *early* cases of gonorrhœa, also in cases of gonococcal arthritis, orchitis or epididymitis, iritis, ophthalmia neonatorum, endocarditis, salpingitis, ovaritis, etc.

A series of seven injections, in conjunction with the usual local treatment, generally suffices for the average case.

The following course of doses is recommended:—

Days.	Injection.	Phials.	5, 10 or 25 c.c. bulk bottles at strength of 50,000 mils. per c.c.	Equivalent in minims from bulk bottles
1	1st injection	5,000 mils.	0·1 c.c.	1·8 minims
4	2nd „	7,500 „	0·15 c.c.	2·7 „
7	3rd „	10,000 „	0·2 c.c.	3·6 „
12	4th „	15,000 „	0·3 c.c.	5·4 „
17	5th „	20,000 „	0·4 c.c.	7·2 „
22	6th „	30,000 „	0·6 c.c.	10·8 „
27	7th „	50,000 „	1 c.c.	18 „

Intervals three to seven days.

It is advisable, when using the foregoing variety of vaccine, to specify "Detoxicated gonococcal vaccine A," to avoid possibility of error. The use of the

course in early cases of gonorrhœa has practically obliterated the incidence of gonorrhœal rheumatism and other systemic complications.

Detoxicated Gonococcal Vaccine plus Secondary Organisms (B). (Telegraphic code: "Mixgon.")

This vaccine is composed of equal parts of the above vaccine A, and the organisms found as secondary invaders in cases of gonorrhœa of more than three or four weeks' duration. It is indicated in old-standing chronic cases in combination with prostatic massage and other treatment.

The secondary organisms contained are:—Staphylococci, Streptococci, Diphtheroids, Pneumococci, B. coli, etc.

The injections are the same as in the case of Detoxicated Gonococcal Vaccine A.

Special Gonococcal Products for Diagnosis and Test of Cure

Gonococcal Proteoses. (A non-toxic provocative cure test for latent gonorrhœa.)

TECHNIQUE.—Inject $\frac{1}{2}$ to 1 c.c. of the proteose subcutaneously and ask the patient to return for examination within 48 hours. He should retain his urine for four hours. The existence of latent gonorrhœa is manifested either by a return of the discharge, or by an increase of shreds in the urine. After such a provocative injection, gonococci often reappear in the discharge.

Absence of any such aggravating symptoms within 48 hours after the injection is of great value in determining that the patient is finally cured.

Gonococcal proteoses are non-toxic and harmless, and the injection has the value of producing a certain amount of immunity, since successive injections of the proteose are followed by a gradually diminishing provocative action. In fact, like the detoxicated vaccine, repeated injections of the proteose tend to dry up an existent discharge.

This test is invaluable as a test of cure at the termination of treatment of all gonorrhœal cases.

Gonococcal Antigen:—In view of the unsatisfactory results obtained in the complement fixation test for gonorrhœa, due to the unsuitability of the antigen used, we have produced a highly efficient compound antigen prepared from upwards of fifty strains of gonococci. This new antigen is standardised to a strength of 3,000 millions per c.c., and has been perfected by bringing it to the optimum hydrogen ion concentration. Full technique for this test is described in Special Report No. 19, Medical Research Committee, a pamphlet published by His Majesty's Stationery Office, Imperial House, Kingsway, London, W.C.2.

We put up this antigen in 1 c.c. phials, strength 3,000 millions per c.c. For use in the blood test it should be diluted one part to nine parts of normal saline. Each phial, therefore, contains sufficient for at least twenty blood tests. It should not be kept more than two days after dilution.

New Detoxicated Anti-Coryza Vaccine.

(Telegraphic code: "Nocold.")

This vaccine contains:—

<i>New Organisms</i>	10,000	million per c.c.
<i>B. pneumosintes</i>	5,000	" " "
<i>Pneumocci</i> (four types)	5,000	" " "
<i>M. catarrhalis</i>	5,000	" " "
<i>B. Friedlander</i>	5,000	" " "
<i>B. septus Hofmann</i>	5,600	" " "
<i>Staphylococci</i>	5,000	" " "
<i>Hæmolytic streptococci</i>	5,000	" " "
<i>B. influenzae</i> (Pfeiffer)	5,000	" " "
TOTAL ..	50,000	million per c.c.

Indicated for the prevention of colds in susceptible persons, also for the treatment of coryza, bronchitis, re-current colds, hay-fever, etc.

Dosage for prophylaxis:—

1st injection	10,000 millions
2nd injection	20,000 "
3rd injection	50,000 "

Interval between prophylactic injections should be seven days.

Dosage for treatment of an acute case:—

1st injection	5,000 millions	} Four to five day intervals.
2nd injection	10,000 "	
3rd injection	20,000 "	

For chronic nasal catarrh or chronic bronchitis a prolonged course of treatment amounting to ten or twelve injections may be required, and the dosage should be gradually increased up to 100,000 millions.

New Detoxicated Anti -Influenza Vaccine.

(Telegraphic code: "Aflaw.")

This vaccine is recommended for the prevention of influenza, especially during epidemics. It is also useful in smaller doses for the treatment of patients actually suffering from this malady.

It contains in equal parts:—

<i>B. pneumosintes</i>		10,000	mils. per c.c.
<i>B. influenza</i> (Pfeiffer)		10,000	" " "
<i>Pneumococcus</i> (types I., II., III. & IV.)		10,000	" " "
<i>Hæmolytic streptococcus</i>		10,000	" " "
TOTAL		40,000	mils. per c.c.

Dosage for prophylaxis:—

1st injection	10,000 millions	} Intervals
2nd injection	20,000 "	
3rd injection	40,000 "	
		of one week.

Dosage for treatment:—

Half the above at intervals of three to four days.

Detoxicated Pneumococcal Vaccine (Polyvalent). (Telegraphic code: "Newmo.")

This vaccine contains the four types of pneumococci and is suitable for the prevention of pneumonia in susceptible persons, also for the treatment of acute pneumonia and pneumococcal nasal catarrh and bronchitis.

Dosage for prophylaxis:—

1st injection	10,000 millions	} Intervals
2nd injection	20,000 "	
3rd injection	40,000 "	
		of seven days.

Dosage for treatment:—

Commence with 1,000 millions in acute cases, and increase cautiously. Intervals, three to four days. In chronic cases commence with 5,000 millions and work up gradually to large doses. In many cases it is possible to work up to 50,000 or 100,000 millions without much reaction. Intervals, five to seven days.

Detoxicated Anti-Typhoid Inoculation

(Telegraphic code: "Tab.")

This vaccine contains equal parts of *B. typhosus*, *B. paratyphosus* A., and *B. paratyphosus* B. It is suitable for the prevention and treatment of typhoid fever.

Dosage for prophylaxis:—

1st injection	10,000 millions	}	Ten days' interval.
2nd injection	20,000 ,,		

Dosage for treatment:—

1st injection	500 millions	}	Intervals of four to five days.
2nd injection	1,000 ,,		
3rd injection	2,000 ,,		
4th injection	5,000 ,,		
etc.			

Detoxicated *B. coli* Vaccine (Polyvalent)

(Telegraphic code: "Beecee.")

Suitable for the treatment of *B. coli* bacilluria, pyelitis, cystitis, colitis, etc.

Dosage:—

1st injection	5,000 millions	}	Intervals of four to five days.
2nd injection	7,500 „		
3rd injection	10,000 „		
4th injection	20,000 „		
5th injection	30,000 „		
6th injection	50,000 „		

NOTE.—*B. coli* infections are often very persistent and chronic, and a prolonged course of 10 to 12 injections may be required. In many cases larger doses than the above can be administered.

Detoxicated Staphylococcal Vaccine (Polyvalent). (Telegraphic code: "Stafboy.")

Suitable for the treatment of furunculosis, boils, abscesses, etc.

Dosage:—Commence with a dose of 5,000 millions and work up rapidly by doubling every five days until a maximum dose of 50,000 millions is reached. As a general rule it is very non-toxic.

Detoxicated Streptococcal Vaccine (Polyvalent). Telegraphic code: "Streps.")

Suitable for the treatment of acute local streptococcal infections, streptococcal septicæmia, puerperal fever, etc.

Dosage:—

1st injection	1,000 millions	}	Intervals of three to five days.
2nd injection	2,000 „		
3rd injection	5,000 „		
4th injection	10,000 „		
5th injection	20,000 „		

Detoxicated Vaccine for Pyorrhœa and Rheumatic Conditions. (Telegraphic code: "Pyrrue.")

This vaccine contains *M. rheumaticus*, *Streptococcus pyogenes*, *Streptococcus fæcalis* and *B. coli*.

It is suitable for the treatment of pyorrhœa, and rheumatic affections, such as acute and chronic rheumatism and rheumatoid arthritis.

Dosage:—

1st injection	5,000 millions	}	Intervals of five to seven days.
2nd injection	10,000 "		
3rd injection	15,000 "		
4th injection	20,000 "		
5th injection	30,000 "		
6th injection	50,000 "		

The foregoing dosage may be increased more rapidly in chronic cases.

Detoxicated Meningococcal Vaccine (contains four types). (Telegraphic code: "Mening.")

For the prevention and treatment of cerebro-spinal fever.

Dosage for prophylaxis during epidemics:—

1st injection	5,000 millions	}	Intervals of seven days.
2nd injection	10,000 "		

Dosage for treatment:—

1st injection, 500 millions, and work up by doubling if there is no reaction, at intervals of four to five days.

It should be given in conjunction with anti-meningococcal serum.

Detoxicated Acne Vaccine. (Polyvalent)

(Telegraphic code: "Dav.")

Contains four parts *Staphylococcus albus* and one part *B. acne*. It is suitable for the treatment of acne.

1st dose, 5,000 millions, and increase gradually, at intervals of five and seven days, up to 50,000 millions.

Detoxicated Streptococcus Scarlatinæ and Secondary Organisms for the Prevention and Treatment of Complications in Scarlet Fever.

This vaccine is put up in rubber capped bottles containing 5 c.c., 10 c.c., and 25 c.c., in a strength of 30,000 millions per c.c.

Dosage for prophylaxis:—

1st injection	5,000 millions	}	Intervals
2nd injection	10,000 ,,		of one
3rd injection	20,000 ,,		week.
4th injection	30,000 ,,		

Dosage for treatment:—

Half the above at intervals of three or four days.

Dosage for children in proportion to body weight, see dosage for infants and children, page 16.

Detoxicated Secondary Organisms (Measles) for the Prevention and Treatment of Complications in Measles.

Dosage: Same as for prevention and treatment of complications in Scarlet Fever.

Detoxicated Tubercle Bacillus Vaccine. (Polyvalent). (Telegraphic code: "Teebee.")

This vaccine is prepared from a number of virulent strains of human type and is composed of all the fractions of the bacillus except the endotoxin.

For the convenience of users this vaccine is now supplied in three strengths, viz. :—

1 c.c. - 100 millions.

1 c.c. - 1,000 ,,

1 c.c. - 10,000 ,,

from which a dose of any size within these limits may be obtained by means of a 1 c.c. graduated hypodermic syringe.

Dosage:—For cases without fever the initial dose should be 10 millions, doubling this amount in the absence of reaction every three to five days until a dose of 500 millions has been reached, when the increases should be made cautiously until maximum doses of 1 c.c. are attained.

Should a reaction occur it is advisable to increase the interval before the next dose by one or more days according to the severity of the reaction, and repeat the dose or even diminish it if the reaction is at all violent. Should this smaller dose still produce a rise of temperature it would be better to wait a week or two and commence again with a very small dose.

It is essential that the temperature be carefully recorded during the treatment, as the information obtained from it is of the greatest value in arranging increases and spacing of dosage.

While the presence of fever is not an absolute contradiction we advise, however, that the vaccine should be used in febrile cases with considerable care owing to the difficulty of determining accurately the amount of reaction should any occur. In some cases it is better to wait until the temperature is normal before commencing a course of detoxicated tubercle bacillus vaccine. The temperature may often be brought to normal by a preliminary treatment with a detoxicated autogenous vaccine prepared from the secondary invaders.

Detoxicated B. diphtheriæ (Klebs-Loeffler) Vaccine. (Polyvalent), for use in clearing up carrier cases.

The initial dose for an adult is 5,000 millions, increasing by doubling until 100,000 millions is reached, when the increases should be made by 50,000 millions. The course should be controlled by bacteriological examination, and experience shows that in very resistant cases it may be necessary to increase the dose to 350,000 millions to obtain satisfactory results.

This vaccine is at present supplied in bulk bottles only, and is standardised to contain the equivalent of 100,000 millions germs per c.c.

Detoxicated Whooping Cough Vaccine.

Contains: B. pertussis, Bordet.	Two parts.
B. influenzæ, Pfeiffer.	One part.
Pneumococci.	One part.

Doses for adults and children above 14:—

1st injection	5,000 millions
2nd injection	10,000 „
3rd injection	20,000 „

For younger children the dose should be reduced in accordance with the body weight, commencing at about one-tenth of the above. It has been found that this vaccine is very well borne, and doses considerably larger than these can be given with advantage for the continuation of treatment if desired.

Detoxicated Actinomyces (Discomyces) Vaccine. (2 mgm. and 20 mgm. per c.c.)

This vaccine has been prepared from a strain of *Actinomyces (Discomyces) bovis* isolated from a human case. It has been tried on several cases in doses commencing at one-tenth of a c.c. of the weaker strength. No reaction has ever been produced, but considerable improvement has followed its administration.

Detoxicated Malta Fever Vaccine.

This vaccine has been used with success in Malta fever cases in S. Africa. The initial dose should be about 1,000 millions, increasing gradually up to 20,000 millions.

Other Detoxicated Vaccines.

- B. dysenteriae, Shiga
- B. dysenteriae, Flexner
- B. enteritidis, Gærtner
- M. melitensis
- M. paramelitensis
- B. pyocyaneus

Prices of Detoxicated Vaccines

Prepared in the "Pickett-Thomson" Research Laboratory
for Genatosan, Ltd.

Detoxicated Gonococcus Vaccine A & B.

Phials, 1 c.c., containing 5,000 or 7,500 mils. ..	0	3	0
,, 1 c.c., ,, 10,000 mils. and upwards ..	0	4	0
Bottles, 5 c.c. (50,000 mils. per c.c.)	1	0	0
,, 10 c.c. ,, ,, ,,	2	0	0
,, 25 c.c. ,, ,, ,,	5	0	0

Detoxicated Anti-Influenza Vaccine.

Phials, 1 c.c., containing 5,000 or 10,000 mils. ..	0	3	0
,, 1 c.c., ,, 20,000 mils. and upwards ..	0	3	6
Bottles, 5 c.c. (40,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Anti-Coryza Vaccine.

Phials, 1 c.c., containing 5,000, 10,000 or 20,000 mils. ..	0	3	0
,, 1 c.c., ,, 50,000 mils.	0	3	6
Bottles, 5 c.c. (50 000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Pneumococcus Vaccine.

Phials, 1 c.c., containing 1,000, 2,000, 3,000, 5,000, 10,000 or 20,000 mils. ..	0	3	0
,, 1 c.c., ,, 40,000 mils.	0	3	6
Bottles 5 c.c. (40,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Anti-Typhoid Inoculation.

Phials 1 c.c. containing 500, 1,000, 2,000, 5,000 or 10,000 mils. ..	0	3	0
,, 1 c.c., ,, 20,000 mils.	0	3	6
Bottles 5 c.c. (20 000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated B. Coli Vaccine.

Phials, 1 c.c., containing 5,000, 7,500 or 10,000 mils.	0	3	0
,, 1 c.c., ,, 20,000, 30,000 or mils.	0	3	6
Bottles, 5 c.c. (50,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Staphylococcus Vaccine.

Phials, 1 c.c., containing 5,000, 10,000 or 20,000 mils.	0	3	0
,, 1 c.c. ,, 40,000 or 50,000 mils. ..	0	3	6
Bottles, 5 c.c. (50,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Streptococcus Vaccine.

Phials, 1 c.c., containing 1,000, 2,000, 5,000 or 10,000 mils. ..	0	3	0
,, 1 c.c., ,, 20,000 mils.	0	3	6
Bottles, 5 c.c. (20,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Pyorrhoea and Arthritis Vaccine.

Phials, 1 c.c., containing 5,000, 10,000, 15,000 or 20,000 mils. ..	0	3	0
,, 1 c.c., ,, 30,000 or 50,000 mils. ..	0	3	6
Bottles, 5 c.c. (50,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Meningococcal Vaccine.

Phials, 1 c.c., containing 500 to 5,000 mils. ..	0	3	0
,, 1 c.c., ,, 10,000 mils.	0	3	6
Bottles, 5 c.c. (10,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Acne Vaccine.

Phials, 1 c.c., containing 5,000 or 10,000 mils. ..	0	3	0
,, 1 c.c., ,, 20,000 mils. and upwards ..	0	3	6
Bottles, 5 c.c. (50,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated B. Pertussis Vaccine (Whooping Cough).

Phials, 1 c.c., containing 5,000 or 10,000 mils. ..	0	3	0
,, 1 c.c., ,, 20,000 mils.	0	3	6
Bottles, 5 c.c. (20,000 mils. per c.c.)	0	17	6
,, 10 c.c. ,, ,, ,,	1	13	0
,, 25 c.c. ,, ,, ,,	4	0	0

Detoxicated Streptococcus Scarlatinae & Secondary Organisms Vaccine.

Bottles, 5 c.c. (30,000 per c.c.)	..	..	..	0	17	6
,, 10 c.c. ,, ,, ,,	..	..	..	1	13	0
,, 25 c.c. ,, ,, ,,	..	..	..	4	0	0

Detoxicated Secondary Organisms Measles Vaccine.

Bottles, 5 c.c. (30,000 mils. per c.c.)	..	..	0	17	6
,, 10 c.c. ,, ,, ,,	..	..	1	13	0
,, 25 c.c. ,, ,, ,,	..	..	4	0	0

Detoxicated Tubercle Bacillus Vaccine.

100 Millions per c.c.

Phials containing 1 c.c.	..	..	..	0	2	6
Bottles ,, 5 c.c.	..	..	..	0	10	0
,, ,, 10 c.c.	..	..	..	0	15	0
,, ,, 25 c.c.	..	..	..	2	0	0

1,000 Millions per c.c.

Phials containing 1 c.c.	..	..	..	0	3	0
Bottles ,, 5 c.c.	..	..	..	0	15	0
,, ,, 10 c.c.	..	..	..	1	0	0
,, ,, 25 c.c.	..	..	..	2	10	0

10,000 Millions per c.c.

Phials containing 1 c.c.	..	..	..	0	4	0
Bottles ,, 5 c.c.	..	..	..	1	0	0
,, ,, 10 c.c.	..	..	..	2	0	0
,, ,, 25 c.c.	..	..	..	5	0	0

Detoxicated Actinomyces (Discomyces) Vaccine.

Bottles, 5 c.c. (4 milligrams per c.c.)	..	..	0	17	6
,, 10 c.c. ,, ,, ,,	..	..	1	13	0
,, 25 c.c. ,, ,, ,,	..	..	4	0	0

Detoxicated B. Diphtheria (Klebs Loeffler) Vaccine.

Bottles, 5 c.c. (100,000 mils. per c.c.)	..	..	0	17	6
,, 10 c.c. ,, ,, ,,	..	..	1	13	0
,, 25 c.c. ,, ,, ,,	..	..	4	0	0

Detoxicated Malta Fever Vaccine.

Bottles, 5 c.c., containing 20,000 mils. per c.c.	..	..	0	17	6
,, 10 c.c., ,, ,, ,,	..	..	1	13	0
,, 25 c.c., ,, ,, ,,	..	..	4	0	0

Detoxicated Gonococcus Proteoses.

Phials, 1 c.c., containing 20,000 mils. per c.c.	..	0	4	0
Bottles, 5 c.c.,	..	1	0	0
,, 10 c.c.,	..	2	0	0
,, 25 c.c.,	..	5	0	0

Gonococcus Antigen, for use in the complement fixation test.

Phials, 1 c.c., containing 3,000 mils. per c.c.	..	0	3	0
Bottles, 10 c.c.,	..	1	7	6
,, 25 c.c.,	..	3	0	0

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PRINTED IN ENGLAND.

